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Title of Project: Enabling Shared Decision Making to Reduce Harm from Drug Interactions: An End-to-End Demonstration

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Structured Abstract

Purpose: The project used emerging CDS standards (**CQL**, **CDS Hooks**, and **SMART on FHIR**) and a learning health community (**CDS Connect**) to enable: (i) clinical decision support for potential drug-drug interactions (DDIs); and (ii) create a shared decision making (SDM) tool for drug-drug interactions to enable clinicians and patients to jointly determine the most appropriate actions to mitigate potential harm.

Scope: Develop a SMART on FHIR app to represent risks associated with gastrointestinal bleeding for patients taking warfarin and non-steroidal anti-inflammatory drugs for SDM. In addition, we developed tools for the CDS Connect community to implement drug-drug interaction artifacts to improve warnings concerning potential risks associated with interacting medications.

Methods: A user-centered process was conducted to design and test usability of a novel SDM called DDInteract. Time to task completion was evaluated across a range of activities using DDInteract. One a stable prototype was developed; a formative evaluation was conducted using physician/patient dyads and a simulated encounter. Dyads were randomized to either DDInteract or usual care. Data was collected from both physicians and patients concerning their opinions about DDInteract or usual care. Measure of interest included the Unified Theory of Acceptance and Use of Technology, the System Usability Scale, the NASATask Load Index; the SDM-9, behavioral intentions; and participant demographics. We also worked with the CDS Connect community to enhance authoring tools to support drug-drug interaction algorithms.

Results: Four patient participants who were 65-85 years old and had taken warfarin for more than five years completed the usability evaluation. A total of 11 clinicians participated in the usability evaluation. The mean time (standard deviation) to complete eight tasks was 144 seconds (74). Screen capture was used to determine how participants navigated through the tool. Eleven participants completed the usability and satisfaction survey, with an overall mean (standard deviation) rating of 4.32 (0.52) out of 5. From the formative evaluation, clinicians who were exposed to DDInteract were significantly more likely to indicate that DDInteract was more logical, efficient, helpful/effective, SDM was valuable, the tool was valuable, and easy to use, compared to usual care traditional DDI tools. DDInteract was generally positively received by both patients and physicians, as stated by one participate: "I really like it. Whenever I can, I like to show something visual while taking to the patient. It is very user friendly, simple, it is not overly complicated."

For CDS Connect aspects of the study, we designed extensions to the authoring tool to add the ability for authors to specify EHR workflow integration points as a part of medication ordering CDS Hooks and support the patient-view, order-select, and order-review hooks. The design adds the ability for authors to specify possible EHR actions within a CDS Hooks service response (known as cards) for the order-select and order-review hooks.

Key Words: Shared decision making, drug-drug interactions, SMART on FHIR, warfarin, non-steroidal anti-inflammatory drugs

Purpose

Drug-drug interactions (DDIs) are preventable adverse events that are responsible for 5–14% of adverse drug reactions (ADRs) in hospitalized patients, are a major risk factor for hospitalization, and occur in up to 13% of elderly ambulatory patients. Exposure to life-threatening DDIs continues to occur despite the widespread use of clinical decision support systems (CDS). The overarching goal of this study was to advance the DDI CDS frontier beyond physician-centered approach to a patient-centered shared decision making model where by physicians and their patients consider the risks of various treatment options. Our central objective was that interoperable sharable decision tools will enhance patient-provider decision making regarding using medications that may interact. The specific aims of this project were:
Aim 1: Design and evaluate a user-centered DDI CDS dashboard called DDInteract;
Aim 2: Enable the creation of contextual DDI CDS knowledge artifacts using the CDS Connect Authoring Tool; and
Aim 3: Conduct a pilot dissemination of DDInteract and the DDI knowledge process.

Scope

The primary scope of activities of this grant are outlined below under each specific aim.

Aim 1: ***Design and evaluate a user-centered DDI CDS dashboard called DDInteract***
Problem: There currently is no technology designed specifically to help patients and providers work together to determine the most appropriate actions to mitigate potential harm from the prescription of a potential anticoagulant DDIs. *Solution:* Using a user-centered design approach that incorporates both provider and patient input, we developed a high-fidelity prototype dashboard as an EHR SMART on FHIR app for shared decision making about potential anticoagulant DDIs called **DDInteract**. We conducted formative evaluations of the tool using patient-physician dyads in a simulated outpatient setting with case vignettes comparing providers' and patients' shared decision making (SDM) quality when using DDInteract versus conventional DDI information sources.

Aim 2: ***Enable the creation of contextual DDI CDS knowledge artifacts using the CDS Connect Authoring Tool***
Problem: Current DDI CDS rules are difficult to exchange, review, and update. This motivates the need for tools to help author and publish interoperable DDI CDS knowledge artifacts. *Solution:* We enhanced the CDS Connect Authoring Tool to support the development of DDI CDS rules for anticoagulant medications using Clinical Quality Language (CQL). CDS knowledge artifacts were validated and published to the CDS Connect Repository. We engaged clinical experts with DDI knowledge but little programming experience in a think-aloud evaluation of the usability of the enhanced CDS Connect Authoring Tool.

Aim 3: ***Conduct a pilot dissemination of DDInteract and the DDI knowledge process***
Problem: Successful adoption and use of novel sharable decision tools requires careful consideration of stakeholder requirements and workflows. *Solution:* We engaged stakeholders to evaluate **DDInteract**. We sought feedback from clinicians, pharmacists, pharmacy informatics personnel, and chief medical informatics officers (CMIOs). We also integrated DDInteract with the Logica public sandbox EHR using **CDS Hooks** and **SMART on FHIR**, and promoted our open-source solutions using a demonstration site and the Patient-Centered Clinical Decision Support Learning Network.

The project aligned with the Agency for Healthcare Research and Quality mission and research priorities by improving the quality and safety of health care.

Methods

Aim 1: The initial activities associated with developing a shared-decision making (SDM) tool for drug-drug interactions was to design and conduct a usability assessment of DDInteract.

Design and Usability: A description of the methods and results are provided in brief below, with full details available in the publication by Reese et al. in *JMIR Human Factors* (see work product below for citation). The design and usability assessment of DDInteract was guided by user-centered design principles and a SDM framework. The user-centered process included iterative and overlapping steps of prototyping (i.e., low-fidelity, stable, and high-fidelity), stakeholder feedback, and usability heuristics and testing. The SDM framework consists of five steps: 1) Seek your patient's participation, 2) Help your patient explore and compare treatment options, 3) Assess your patient's values and preferences, 4) Reach a decision with your patient, and 5) Evaluate your patient's decision.[25] Figure 1 depicts a summary of the design and usability process.

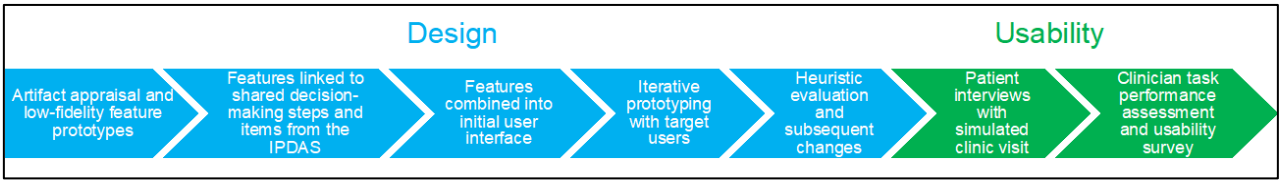


Figure 1. Summary of the design and usability process for DDInteract. IPDAS, International Patient Decision Aid Standards Collaboration.

Target users (i.e., two physicians and one pharmacist) were individually shown the initial complete user interface prototype and asked to provide feedback on the usefulness, aesthetics, proposed functionality, and content. We went through several iterations in collaboration with these target users until no additional feedback was offered. At this point the prototype was considered stable enough for a heuristic evaluation. The heuristic evaluation was based on knowledge of Jakob Nelson's 10 Usability Heuristics for User Interface Design and was performed by two experts with training and experience in human centered design, psychology, and medical informatics. The goal of heuristic evaluation was to identify design flaws that could be addressed prior to conducting resource-intensive testing. Specific feedback regarding design that might impede the user's goals were noted and shared in a team meeting, along with a discussion of potential solutions for each flaw. After modifying the stable prototype to address findings from the heuristic evaluation, we considered it high-fidelity and ready for usability testing.

Usability assessments comprised two parts: (i) patient interviews with simulated clinic visits and (ii) clinician task performance assessments and usability surveys. We designed DDInteract for clinicians to use at the point of care. Because patients would not use DDInteract without a clinician present, we did not test task completion success and efficiency with patients. We recruited patient participants from the anticoagulation and cardiovascular services at the University of Utah. Inclusion criteria required participants to be on warfarin for a chronic condition, such as atrial fibrillation. We assessed each participant's perceived usability and usefulness of DDInteract was assessed with participants individually through two simulated clinical scenarios and a semi-structured interview. Participants received two short clinical vignettes to read before the session. The vignettes tested the range of responses based on a patient's risk (i.e., high risk and low risk) of gastrointestinal (GI) bleeding. In the high-risk vignette, the patient had multiple risk factors for GI bleeding including age greater than 65, use of an antidepressant, and history of a GI bleeding. In the low-risk vignette, warfarin was the only risk factor. Participants simulated SDM based on the clinical vignettes with a provider author. Following the clinical scenarios, patients answered questions pertaining to aspects of DDInteract, the use of DDInteract for SDM, and the utility of SDM for DDIs. The interviews occurred online with audio and screen recording. We transcribed and coded the audio into general topics.

We recruited physicians and pharmacists with anticoagulation therapy experience using snowball sampling. The overarching goal of the clinician usability assessment was to obtain objective and subjective

data on the use of DDInteract. Participants completed a task performance assessment and a perceived usefulness survey. Participant characteristics were also collected as part of the survey. Participants received links to the instructional video, task performance assessment, and survey by emailed. The instructional video was a brief introduction to DDInteract. The task performance assessment was web-based and recorded the participant's screen. The survey was based on the System Usability Scale (SUS) and included a free-text section for feedback. Tasks comprised eight key navigation and functionality tasks (Table 1). We measured performance by task completion rates and the time to complete each task. After a task was completed, the application reset to the home screen. Completion time was measured from when the home screen was displayed to when the task was completed.

Table 1. Clinician task prompts and actions performed that result in successful completion.

	Tasks	Success
1.	Your patient has questions about what a gastrointestinal bleed is. Please navigate to patient education about a gastrointestinal bleeding.	Navigating to and clicking on the dropdown arrow for "What is a gastrointestinal (Stomach) bleed?"
2.	With previous patients, you have found it confusing for them to understand the drug class NSAIDs. Please find the picture of multiple NSAIDs to illustrate how not only ibuprofen is an NSAID.	Navigating through the "What is a drug-drug interaction" dropdown and clicking on the "NSAID" hyperlink.
3.	Your patient informed you that they stopped taking fluoxetine. Please remove fluoxetine (Prozac) as a risk factor to show how their risk has changed.	In the patient Risk Profile section, the toggle for "On Selective Serotonin Reuptake Inhibitor" was pre-configured in the on position. The successful action was clicking the toggle off.
4.	Assume your patient would like to take a medication then click the button to view medication options.	Navigating to the decision-tree questions and clicking on the "Medication" button.
5.	Your patient has decided to try non-NSAID medication options. Please select acetaminophen (Tylenol) and lidocaine (Lidoderm).	Navigating to the second question of the decision-tree and clicking "Other medications" then selecting "acetaminophen (Tylenol) 500mg" and "lidocaine (Lidoderm) 5% patch."
6.	Your patient believes NSAIDs help the most with pain but would like to reduce their risk. Please select the Oral NSAID option with the least gastrointestinal bleed risk. Then select that a stomach acid reducer is not needed.	Navigating to the second question of the decision tree and clicking on "Oral NSAID" then selecting "celecoxib."
7.	Your patient insists on taking medications only once per day. Please select the Oral NSAID option with the most risk and add esomeprazole (Nexium).	Navigating to the second question of the decision tree and clicking on "Oral NSAID" and selecting "meloxicam." Then clicking on "Stomach acid reducer" and selecting "esomeprazole."
8.	Please place any order in the queue for one of the treatment options.	Navigating through the decision tree and clicking "Accept."

Formal Evaluation: A formal evaluation of DDInteract was conducted to evaluate the performance of the SDM tool through simulated encounters where physicians/patient dyads worked on a SDM task based on case vignettes. Physician/patient dyads were randomly assigned to proceed as usual care or to use or DDInteract. Physicians on both groups (intervention or control) could use conventional DDI alert such as Web DDI checkers with a narrative summary of the interaction, along with a link to a full technical description within a drug knowledge resource (e.g., Micromedex®, UptoDate®, etc.).

We integrated DDInteract with the sandbox EHR environment provided by Logica using SMART on FHIR. We recruited providers to explore the use of DDInteract through a guided discussion by an investigator. After completing the simulated visit, they were asked to complete an online survey regarding the tool.

Physicians randomized to the DDInteract group were sent an email with a link to a video explaining how to use DDInteract. Physicians randomized to usual care were educated about the procedures and goal of the simulation and provided links to DDI web-based tools to resources for DDIs. Physicians in both groups were

encouraged to proceed as they would normally interact with a patient, except that physicians who were randomized to DDInteract were asked to use the tool to assist with the encounter. Physicians in both groups were allowed to share their computer screen to show the patients information found on the Web or DDInteract. After the virtual encounter, physicians and patients participated in a semi-structured interview with the research team. Once the session was completed, participants completed an online survey about the simulated visit.

The physician post-simulation assessment contained: 1) items related to usability (6 questions adapted from the System Usability Scale), 2) items of the NASA Task Load Index; 3) 26 questions according to the Unified Theory of Acceptance and Use of Technology (UTAUT) following constructs: performance expectancy, effort expectancy, attitude towards using technology, social influence, facilitating conditions, self-efficacy, anxiety and behavioral; 4) nine items from SDM-9 items scale; 5) seven questions related to perceived behavioral intentions; and 6) data on participant demographics.

Patient participants were asked to compete a survey that included an adaptation of the SUS scale (6 items to score from Strongly Agree to Strongly Disagree) and an 11 item adaptation of the Decisional Conflict Scale (DCS). We also asked participants for demographic information and anticoagulant treatment questions.

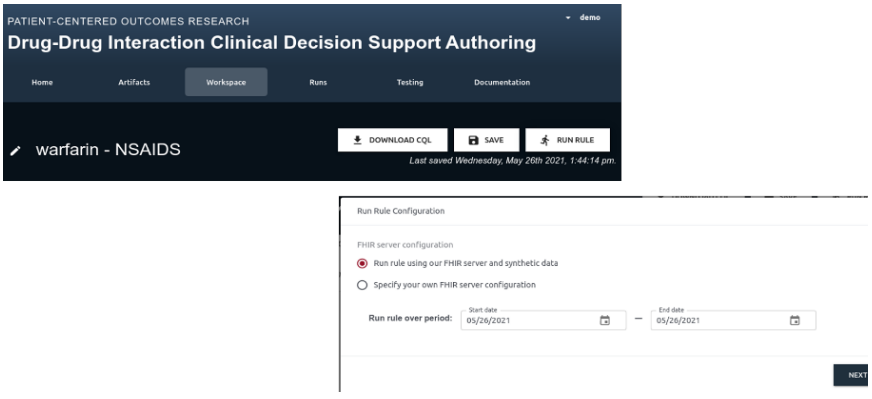
We calculated the mean and standard deviation (SD) for each question/construct. For the primary outcome (shared decision-making quality) in both study hypotheses (physicians and patients respectively), we conducted a two-group Student's t-test to assess differences in ratings on DDInteract versus usual care. A similar approach was used to test for differences in secondary measures, i.e. perceived efficiency, effort, and user experience.

Aim 2: Enable the creation of contextual DDI CDS knowledge artifacts using the CDS Connect Authoring Tool:

We accomplished the goals for Aim 2 as proposed in the grant proposal:

Goal 1: Enhance the CDS Connect Authoring Tool to support authoring DDI CDS rules involving anticoagulant medications: Table 2 shows the new capabilities we developed into our team's branch of the CDS Connect Authoring Tool. The project now supports all of the functionality needed to author DDI CDS rules involving anticoagulant medications in FHIR R4. With input from leading CDS Service developers, we have designed extensions to the Authoring Tool to add the ability for authors to specify EHR workflow integration points as a part of medication ordering CDS Hooks and support the patient-view, order-select, and order-review hooks. The design will also add the ability for authors to specify possible EHR actions within a CDS Hooks service response (known as cards) for the order-select and order-review hooks. We have also implemented functionality for the Authoring Tool interact with a CDS Service to run new CDS rules over real-world data served as FHIR resources (see Figure 2).

Figure 2. The Authoring Tool interface for setting up rule validation using EHR data stored in a FHIR server. In this case, the user has selected to Run Rule which brings up a configuration window that starts the process



We have tested that this feature works using synthetic data hosted in a OMOPonFHIR server. The Authoring Tool helps users to use the feature by enabling them to create a FHIR PlanDefinition resource from CQL knowledge artifacts, associating specific CQL CDS artifacts with event-conditions-action components in a PlanDefinition, posting these resources to a CDS service, and then running a CDS test as a job external to the Authoring Tool user interface.

Figure 3. The next step in the process of configuring how to run the rules for validation on a FHIR server is to specify details of the PlanDefinition resource. This windows also shows the action that the user will be prompted to take for the rule.

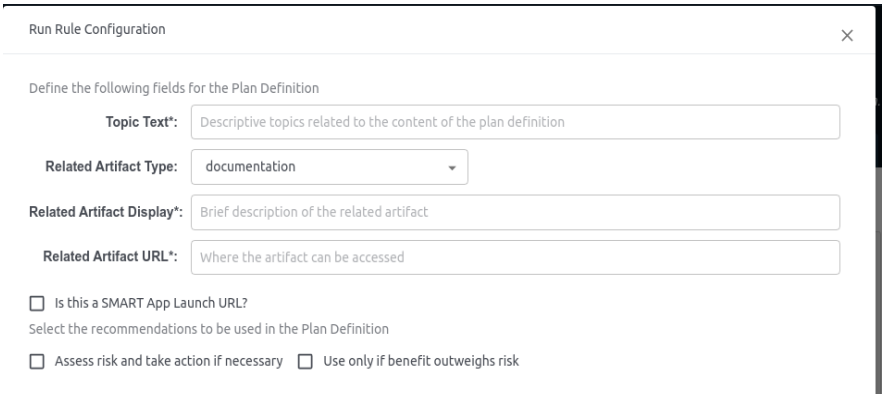
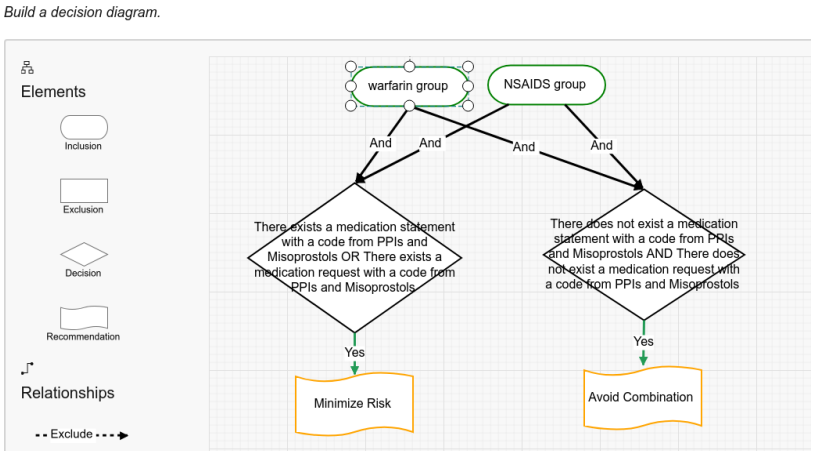


Figure 4. After configuring the FHIR server information and the PlanDefinition resource, the Authoring Tool posts the rule CQL file, PlanDefinition, and value sets to the FHIR server. It then executes a job that runs the rule. The run simulates executing the patient-view hook for every patient who has an encounter in the EHR over the time period. This figure shows the summary information that is returned by the system once the job is done. Clicking 'View By Date' will list each alert that fired over the date range for the alert.

The Authoring Tool provides the user with a summary of alert triggers over the time period that the user specifies for validation. The summary lists the number of patients that would trigger each category of alert and a listing of each alert and its operational classification (see Figures 3, 4, and 5).

Goal 2: Technical validation of the anticoagulant DDI CDS artifacts written in CQL: DDI CDS rules require technical validation to ensure that they are correct and shareable. We used the node-based CQL validation framework to validate two anticoagulant drug-drug interaction artifacts that are now fully available in the CDS Connect Repository. One for warfarin - Nonsteroidal anti-inflammatory drugs (https://cds.ahrq.gov/cdsconnect/artifact/contextual-drug-interaction-decision-support-algorithm-warfarin-nonsteroidal) and the other for warfarin and antidepressants (https://cds.ahrq.gov/cdsconnect/artifact/contextual-drug-interaction-decision-support-algorithm-warfarin-antidepressants). The artifacts released to CDS Connect Repository include the CQL, FHIR libraries, an implementation guide and narrative describing the goals and evidence support for the artifacts. Both are also discussed in recorded webinars accessible at ddi-cds.org. We went further and validated CQL rules for four other potential DDIs (warfarin-salicylates, selective serotonin reuptake inhibitors-thiazide,

Figure 5. Our visual user interface for authoring DDI CDS rules within the CDS Connect Authoring Tool showing a branch of the warfarin-NAIDS rule.



immunosuppressants-fluconazole, and citalopram-QT interval prolongation).

These are in preparation for release to the CDS Connect Repository.

The validated warfarin-NSAIDs CQL artifacts were included in the successfully balloted the HL7 Drug-Drug Interaction Implementation Guide (http://hl7.org/fhir/uv/pddi/2020SEP/). The ballot received over 40 comments from a wide range of stakeholders including regulatory (FDA), EHR vendor (Epic and Cerner), health systems (VA), and professional organizations (AMA). We are in the process of reconciling the ballot comments so that the standard can be approved.

Goal 3: Conduct think-aloud usability testing of the CDS Authoring Tool with clinical drug experts with little or no programming experience: We made significant progress on a user study to test the usability of the features for drug experts who have little or no training on the use of the Authoring Tool. After implementing several of the extended features described above, we conducted two user interviews focused on the usability of the drug-drug interaction knowledge artifact authoring in the CDS Authoring Tool. These user interviews led to a significant re-design of the user interface to make the authoring workflow more transparent, adjusted the terminology to fit what drug experts more commonly use, and added features that make common tasks for drug interaction knowledge artifacts more intuitive. We then conducted think-aloud sessions to evaluate the usability of the interface.

Drug experts whose work involved writing and maintaining DDI knowledge artifacts were recruited to complete pre-specified DDI CDS rule writing tasks using the enhanced CDS Authoring Tool and the sessions were completed via web conference. Usability sessions were conducted with seven drug experts. At the end of the sessions participants were asked to complete a System Usability Scale (SUS) questionnaire regarding the application (Likert scaled) with 1 being “strongly disagree” and 5 being “strongly agree”. The results of the questionnaire (Table 2) showed that participants felt much more confident using the tool and would be able to learn to use it quickly. While participants did not consider the system unnecessarily complex and that they would like to use it frequently, the study indicated a learning curve.

Table 2. *Averages from the results of the System Usability Scale questionnaire*

Question	Avg.
I would like to use this system frequently	3.83
I found the system unnecessarily complex	2.67
I thought the system was easy to use	3.67
I would need the support of a technical person to use this system	3.17
I think that most people would learn to use this system very quickly	3.67
I found the system very cumbersome to use	2.17
I felt very confident using the system	3.33
I needed to learn a lot of things before I could get going with this system	3.33

We concluded that implementing a diagram-based user interface improved the usability of the CDS Connect Authoring Tool in the realm of CDS rule authoring. It allowed for this novel tool to bridge the gap between domain expertise and rule creation. Additional modifications allowed these rules to be immediately tested against an already existing EHR FHIR server. With this tool, contextual DDI CDS artifacts can now be authored, tested, and shared quicker and easier. We are in the process of conducting another seven interviews with users whose work focuses on maintaining drug interaction alerting systems within healthcare organizations.

Aim 3: To gain acceptance and uptake of these innovative CDS tools, we implemented a multi-faceted dissemination strategy was implemented to create awareness and promote use of DDInteract and related resources. Due to the COVID-19 pandemic we were not able to attend an in-person meeting to demonstrate the DDInteract. However, we conducted a number of activities to disseminate the tool and collect feedback using the DDI-CDS website. We recruited individuals from various organizations to evaluate DDInteract using the web-based version using an online survey. Ads were placed within the monthly newsletter of the Anticoagulation Forum, a specialty organization of clinicians that treat and manage patients receiving anticoagulants. We also sent notices to individuals who had attended one or more webinars associated with the Meaningful Drug Interaction Alerts webinars. Furthermore, we promoted the tool and evaluation through

various list-serves including the American Medical Informatics Association pharmacoinformatics work group, emails to colleagues at other academic medical centers, colleagues associated with another grant focused on patient self-management of warfarin (funded by AHRQ), and the CDS Connect monthly webinar.

In addition, DDInteract has been integrated with the Logica EHR sandbox (formerly the Healthcare Services Platform Consortium) using SMART on FHIR. Logica provides a platform for developers and researchers to test interoperability of third-party applications. We tested the interoperability of DDInteract using the CDS Hooks and EHR sandbox hosted by Logica. In the future, we plan to register DDInteract with the SMART® App Gallery. SMART is an App platform that currently hosts nearly 50 healthcare related apps (https://apps.smarthealthit.org/apps/).

We also reached out to individuals with experience in interoperability and production managers via the major EHR networking groups. Using our professional network and using snowball techniques, we promoted DDInteract to solicit feedback about the SDM CDS.

During monthly webinars for our Meaningful Drug Interaction Alert (MDIA) grant, we encouraged individuals to review and provide feedback on DDInteract. Attendance at these webinars is typically between 70 to 150 individuals. Our experience with the webinars is that representatives from various drug compendia such as First DataBank, Wolters-Kluwer, Gold Standard, and Multum attend the webinar. Disseminating information about DDInteract may have resulted in one or more individuals examining and evaluating the app. Individuals viewing the DDInteract app were presented with a pop-up with links to a survey about DDInteract. Respondents were offered a chance to win one of ten $100 Amazon gift cards. Respondents completing the assessment of DDInteract answered questions based on the UTAUT pertaining to the constructs of performance expectancy, effort expectancy, attitude toward using the technology, social influence, self-efficacy, facilitating conditions, anxiety, and behavior intention.

Results

Usability: Four patient participants who were 65-85 years old and had taken warfarin for more than five years completed the usability evaluation. For the high-risk vignette (patient with multiple risk factors), all participants chose a combination of non-medication treatment (e.g., physical therapy) and acetaminophen. For the low-risk scenario (patient with minimal risk factors), most participants chose a short course of celecoxib or ibuprofen, with a proton pump inhibitor. While participant knowledge about the warfarin-NSAID DDI varied, all participants appreciated the ability to view the DDInteract app while the provider discussed risk and treatment options. One participant stated, *"If I wasn't able to see the [treatment] options, I wouldn't know what to ask."* Furthermore, participants felt empowered to participate in making decisions that aligned with their preferences by referring to the decision aid during discussion, *"I personally don't like taking medications and want two avoid taking more. It looks like I can try other ways to relieve my pain and I would prefer trying those."* Participants wanted to have access to the decision aid or a printout, outside the encounter, to review what was discussed and decided. One participant stated, *"I usually forget what we [patient and provider] talked about during the appointment, so I would go to my After Visit Summary to review what we talked about."* Most participants believed SDM was novel and different from past decision-making experiences with providers. *"Doctors usually make decisions like these for me."* Generally, participants valued SDM and using DDInteract with the provider.

A total of 11 clinicians participated in the usability evaluation (Table 3). Three of the eleven participants stopped after the first task. Two of the three participants were pulled to clinical duties. The other participant failed to complete the second task and chose to stop the study, rather than skipping the task. Of the eight participants who completed the study, all were successful on each task. The mean time (standard deviation) to complete eight tasks was 144 seconds (74). Screen capture was used to determine how participants navigated

through the tool. Eleven participants completed the usability and satisfaction survey, with an overall mean (standard deviation) rating of 4.32 (0.52) out of 5. Table 4 delineates mean ratings for each survey item.

Table 3. Participant characteristics for the usability evaluation

	N	Specialty (N)	Participant years of experience				Participant clinical percent effort				Self-assessed Experience with warfarin from 0 to 100
			< 5	6-10	11-15	> 16	< 21	21-40	61-80	> 80	Mean (range)
Physicians	7	Family Medicine (4), Emergency / Critical care (2), Hematology (1)	2	2	2	1		2	3	2	67 (29-88)
Pharmacists	4	Anticoagulation / Ambulatory care (3), General (1)			2	2	1		1	2	93 (87-100)

Table 4 provides responses from clinicians that completed the usability survey items. In general, participants agreed or strongly agreed with statements concerning the usability of DDInteract.

Table 4. Clinician Usability Assessment (n = 11)

Items	Mean (SD)
I found the decision tool to be logical	4.36 (0.67)
I found the decision tool to be efficient	4.18 (0.75)
The decision tool was effective in the decision-making process	4.36 (0.67)
The shared decision making was valuable	4.27 (0.79)
The decision tool was valuable	4.36 (0.67)
I thought the decision tool was easy to use	4.27 (0.65)
I enjoyed the experience	4.36 (0.81)
I learned something new from this experience	4.36 (0.67)

Responses were on a 1-5 Likert scale where 1 = Strongly Disagree and 5 = Strongly Agree.

Formative Evaluation: A total of 12 physician/patient dyads completed the formative simulation evaluation. Six dyads were randomized to DDInteract, and six were randomized to usual care. Results of the formative evaluation are provided in Tables 5 to 10. Table 5 contains results comparing clinicians who used DDInteract versus usual care as measured by the NASA Task Load Index [(scaled from zero (low/easy/successful) to 10 (high/demanding/unsuccessful)]. There was a significant difference with respect to physical effort, but none of the other constructs were significantly different between the groups.

Table 5. NASA Task Load Index for Clinicians

(mean, SD)	*Clinicians*		
	DDInteract	**Control**	***p***
Mental demand	3.8 (0.98)	4.7 (3.2)	0.57
Easy/demanding (Physical effort)	0.8 (0.75)	7.3 (3.7)	0.008
Temporal demand	1.8 (1.6)	3.6 (3.5)	0.28
Effort	2.3 (1.0)	3.6 (2.6)	0.30
Performance	1 (0.9)	1.7 (1.8)	0.45
Total average	2.0 (1.2)	4.2 (2.1)	0.08

Results from the adapted System Usability Scale (SUS) are shown in Table 6 (Likert scaled from 1 to 5). While no significant differences were noted between patients exposed to DDInteract versus usual care, clinicians who were exposed to the DDInteract were significantly more likely to indicate that DDInteract was more logical, efficient, helpful/effective, SDM was valuable, the tool was valuable, and easy to use, compared to usual care traditional DDI tools.

Table 6. Results from the Adapted System Usability Scale (SUS) from Patients and Clinicians

(mean, SD)	**Patients**			**Clinicians**		
	DDInteract	**Control**	***p***	**DDInteract**	**Control**	***p***
It was logical	4.7 (0.5)	4.8 (0.4)	0.65	4.8 (0.4)	3.7 (1.0)	0.03
It was efficient	4.5 (0.5)	4.4 (0.5)	0.77	4.7 (0.5)	3.5(1.0)	0.04
Helpful/effective in the decision-making process	4.7 (0.5)	4.4 (0.9)	0.57	4.5 (0.5)	2.8 (1.2)	0.02
The SDM using the tool was valuable	4.5 (0.5)	4.8 (0.4)	0.26	4.7 (0.5)	2.8 (0.7)	<0.001
The tool was valuable	NA	NA	NA	4.3 (0.5)	2.8 (1.2)	0.02
Easy to use	4.5 (0.5)	4.4 (0.9)	0.83	4.8 (0.4)	3.2 (1.5)	0.04
Enjoyed the experience	4.7 (0.5)	4.8 (0.4)	0.55	NA	NA	NA
Learned something from this experience	4.8 (0.4)	4. 7 (0.8)	0.67	4.5 (0.5)	2.8 (1.7)	0.06

There were no significant differences between patients receiving DDInteract as compared to usual care with respect to attributes related to decision conflict scale (DCS) (See Table 7).

Table 7. Decision Conflict Scale as Assessed by Patients

Attribute	**Patients**		
(strongly agree (1) to strongly disagree (5)	**DDInteract**	**Control**	***p-value***
Decision is hard for me to make	3.3 (1.2)	3.5 (1.4)	0.83
Unsure what to do in this decision	3.7 (1.0)	3. 7 (0.8)	1.00
Clear what choice is best for me	1.8 (0.75)	2.2 (1.2)	0.57
I am aware of the choices I have to protect myself from drug interactions	1.8 (1.7)	1. 7 (0.5)	0.76
I know the benefits of avoiding drug interactions	1. 7 (1.2)	1. 7 (0.8)	1.00
I know the potential for harm for drug interactions	1. 7 (0.8)	1.5 (0.5)	0.69
I need more advice and information about my choices	3 (1.3)	2. 7 (1.2)	0.65

Attribute	Patients		
(strongly agree (1) to strongly disagree (5)	**DDInteract**	**Control**	***p-value***
It's hard for me to decide if the benefits are more important to me than the risks, or opposite	3 (1.3)	3 (1.1)	1.00
I feel I have made an informed choice	1.7 (0.8)	1.8 (0.7)	0.72
My decisions show what is most important for me	1.8 (0.9)	1.7 (0.5)	0.72
I expect to stick with my decision	1.8 (0.9)	2.2 (0.7)	0.53

Evaluation of DDInteract and usual care by clinicians using the UTAUT scale is shown in Table 8. Response scaling of the 7-item Likert scale was reduced to positive, neutral, and negative. In general, across the various constructs participants who were exposed to DDInteract were positive about the app. In contrast, those respondents receiving usual care varied from positive to negative across the constructs except for social influence and self-efficacy. The positive response for social influence for the control participants is likely due to the tools being currently available within the existing EHR systems.

Table 8. Unified Theory of Acceptance and Use of Technology (UTAUT)							
Construct	**Questions**	**DDInteract (N=6)**			**Control (N=6)**		
		Positive	Neutral	Negative	Positive	Neutral	Negative
Performance expectancy	Useful in job	6 (100%)			3 (50%)	1 (17%)	2 (33%)
	Accomplish task more quickly	5 (83%)	1 (17%)		1 (17%)	2 (33%)	3 (50%)
	Increases productivity	2 (33%)	4 (67%)		1 (17%)	1 (17%)	4 (67%)
Effort expectancy	Interaction clear and understandable	6 (100%)			4 (67%)	1 (17%)	1 (17%)
	Easy to become skillful	6 (100%)			5 (83%)		1 (17%)
	Easy to learn to navigate	6 (100%)			4 (67%)		2 (33%)
Attitude towards using technology	Using is a good idea	6 (100%)			4 (67%)		2 (33%)
	Makes work more interesting	3 (50%)	3 (50%)		3 (50%)		3 (50%)
	It is fun	3 (50%)	3 (50%)		2 (33%)	2 (33%)	2 (33%)
	Like working with it	6 (100%)			2 (33%)	2 (33%)	2 (33%)
Social influence	People who influence me think I should use it	5 (83%)	1 (17%)		2 (33%)	2 (33%)	2 (33%)
	People who are important to me think I should use it	4 (67%)	2 (33%)		3 (50%)	1 (17%)	2 (33%)
	Senior management of my organization would be helpful in the use of it	6 (100%)			2 (33%)	2 (33%)	2 (33%)
	My institution would support the use of it	6 (100%)			5 (83%)	1 (17%)	
Self-efficacy	I have the resources necessary to use it	6 (100%)			6 (100%)		
	I have the knowledge necessary to use it	6 (100%)			6 (100%)		
	It is not compatible with other systems I use	1 (17%)	1 (17%)	4 (67%)		2 (33%)	4 (67%)
	There is assistant available for system difficulties with it	2 (33%)	4 (67%)		2 (33%)	1 (17%)	3 (50%)
Facilitating conditions	I could use it if no one was around to tell me what to do as I go	6 (100%)			5 (83%)	1 (17%)	
	I could use it if I could call someone for help if stuck	4 (67%)		2 (33%)	4 (67%)	1 (17%)	1 (17%)
	I could use it if a lot of time to complete the job for which it was provided	2 (33%)	2 (33%)	2 (33%)	5 (83%)		1 (17%)
Anxiety	I feel apprehensive about using it			6 (100%)	1 (17%)	1 (17%)	4 (67%)
	It scares me to think that I could lose a lot of information using it, by hitting the wrong key			6 (100%)			6 (100%)
	I hesitate to use it for fear of mistakes I cannot correct			6 (100%)	2 (33%)	1 (17%)	3 (50%)
	It somewhat intimidates me			6 (100%)	1 (17%)		5 (83%)
Behavioral	I intend to use it in the next 3 months	5 (83%)	1 (17%)		4 (67%)		2 (33%)

Shared decision making was assessed by only clinicians using the SDM-9 questionnaire and the results are shown in Table 9. There was a significant difference between the groups with respect to perceptions of DDInteract as compared to usual care with respect to SDM for all attributes except collaboratively weighing the different treatment options, selecting a treatment option together, and reaching an agreement on how to proceed.

Table 9. Shared Decision Making

SDM-9 items scale	**Providers**		
	DDInteract	**Control**	***p-value***
The tool made clear to my patient that a decision needs to be made.	4.5 (0.8)	3.3 (0.8)	0.034
The tool helped my patient to be involved in making the decision.	5.5 (0.5)	3.2 (1.3)	0.005
The tool provided different options for treating the patient's medical condition.	5.7 (0.5)	1.8 (1.2)	<0.001
The tool provided advantages and disadvantages of the treatment options.	5 (1.1)	2.8 (1.2)	0.007
The tool helped my patient understand all the information.	4.8 (0.4)	2.7 (1.4)	0.009
The tool helped facilitate me I asking my patient which treatment option he/she prefers.	5.2 (0.8)	3 (1.3)	0.007
My patient and I thoroughly weighed the different treatment options.	5 (0)	4.7 (0.8)	0.363
My patient and I selected a treatment option together.	5.2 (0.4)	5 (0.9)	0.690
My patient and I reached an agreement on how to proceed.	5.7 (0.5)	5.3 (0.8)	0.422

Assessment of perceived behavioral control by clinicians is shown in Table 10. Clinicians exposed to DDInteract were more likely to indicate they can share SDM in the clinic as compared to those clinicians randomized to usual care (p=0.02). DDInteract clinicians were also more likely to report that they could conduct SDM without extending the duration of the visit (p=0.03). No other items were significantly different between the two groups.

Table 10. Perceived Behavioral Control

Perceived behavioral control	**Providers** Mean (SD)		
	DDInteract	**Control**	***p***
I am convinced that I can share decision-making in the clinic	6.8 (0.4)	6.0 (6.0)	0.02
I have control over the level of SDM that is accomplished in the clinic	6.2 (0.8)	5.7 (0.5)	0.21
I can perform SDM without extending the duration of the consultation	5.5 (0.5)	3.7 (1.5)	0.03
Knowledge about SDM is important in order to apply SDM	6.5 (0.5)	5.7 (1.4)	0.20
Communication skills are important for SDM	7.0 (0.0)	6.7 (0.5)	0.17
Patients are motivated to participate in SDM	6.0 (0.9)	5.5 (1.2)	0.44
In general patients have enough knowledge, intelligence and understanding needed for SDM	6.0 (0.9)	5.0 (1.7)	0.23
Total	6.3 (0.5)	5.5 (0.9)	0.07
Time constraints are an important issue in SDM	5.7 (0.8)	6.5 (0.5)	0.09

Perceived behavioral control	**Providers** Mean (SD)		
	DDInteract	**Control**	***p***
I have enough knowledge about SDM	6.0 (0.6)	5.7 (0.5)	0.34
I have the communication skills required for SDM	6.0 (0.6)	6.2 (0.8)	0.68
Patient motivation is important for SDM	6.5 (0.8)	5.8 (1.2)	0.28
Patient knowledge, intelligence and understanding is important for SDM	6.3 (0.8)	5.5 (1.6)	0.30

Semi-structured interviews were conducted with participants of both groups after the simulated encounter was completed. In general, DDInteract appeared to be well received by the clinicians. Statements like:

> “I like it, it helps patients visualize the risk instead of me just talking statistics, they see the risk in the more obvious way. I like the intervention there that could reduce the risk of bleeding, you can add more types of bleed as you go, but the idea is excellent"
>
> "I really like it. Whenever I can, I like to show something visual while taking to the patient. It is very user friendly, simple, it is not overly complicated.”
>
> “Iliked using it, how dynamic it is, how it instantaneously adjusted the effects of the different attributes. The tool made me more comfortable with that decision”
>
> “I think it is really nice, it reminds me a lot of the lung screening tool, but, this one was a lot easier to use and translate into practical information than that one.”
>
> "I think overall the tool is a great and helpful. We do thrombosis consultation so much that we don't necessary need to be familiarized with certain elements of it, whereas other physicians might need to be."

Concerns about extra time to use DDInteract were not evident among the participants. As one clinician stated:

> “I am trying to imagine having this conversation without the tool, I don't even think the tool would even make it longer. I think what it does is cut down on having to overly explain things, cut down on the feeling that I have to reemphasize something because it was a visual tool and the patient is seeing what I am seeing so they don't ask for repeating, so I probably save some questions too. In all, I think it would save some time.”

Another clinician perceived the tool would encourage more conversations with the patient and help them understand the risks associated with bleeding and anticoagulation treatment.

> "I think it was fast to use. I see thrombosis patients so I do a lot of counseling about warfarin or anticoagulation. I think I tend to assume that people have already been through the education but this would be nice because it will slow me down and help me actually understand what the risk is, which I might just summarize very quickly. But I think this would be really helpful from a patient standpoint to actually seeing something that explains it a little better.”

When patients were asked about the icon array in DDInteract as an approach to display the risk of bleeding, some comments included:

> "I think seeing the graphic portrayal of the different risk levels and how to treat the pain was very helpful. I think it was well done….. I thought this tool was much more thorough than the information that I've gotten in the normal clinic visit. I did not know the number of bleeds per 100 patients, that has never been discussed with me during my doctor visit"
>
> “The icon array definitely makes sense to me."
>
> “I learn better by what I see.”
>
> “I think the chart with different numbers showing different reactions you get by taking ibuprofen kinda spells it out like black and white for me."

Comments by patients concerning the usual care websites showing drug-drug interactions were also perceived as useful by some patients. Comments included:

> "The information is helpful because a lot of people like to see something written. "
>
> "It is helpful and it gives you a little bit more power, it's not just you sitting there."

List of publications and products

Publications

Reese T, Del Fiol G, Morgan K, Hurwitz J, Kawamoto K, Gomez-Lumbreras A, Brown ML, Thiess H, Vazquez S, Nelson S, Boyce R, Malone DC. Shared decision making for drug-interactions: design and usability of an application for warfarin and non-steroidal anti-inflammatory drugs. *JMIR Human Factors* 2021; 8(4):e28618. Doi: 10.2196/28618.

Thiess H, Del Fiol G, Malone D, Cornia R, Sibilla M, Rhodes B, Boyce R, Kawamoto K, Reese TJ. Coordinated Use of Health Level 7 Standards to Support Clinical Decision Support: Case Study with Shared Decision Making and Drug-Drug Interactions. *International Journal of Medical Informatics*. Submitted August 2021; In review.

HL7 Clinical Decision Support Workgroup. Potential Drug-Drug Interaction (PDDI) CDS IG; Implementation Guide; HL7, Balloted September, 2020.

Presentations

Thomas J Reese. Shared Decision Making for Drug Interactions: Design and Usability of an Application for Warfarin and Non-steroidal Anti-inflammatory Drugs. Podium presentation, Clinical Informatics Conference (CIC), May 2021.

Thomas J Reese. Shared Decision Making for Drug Interactions: Design and Usability of an Application for Warfarin and Non-steroidal Anti-inflammatory Drugs. American Medical Informatics Association (AMIA), Clinical Decision Support Work Group presentation, April 2021.

Malone DC, Boyce RD. 2019 Annual Conference of the Patient-centered Clinical Decision Support Learning Network. Enabling Shared Decision Making to Reduce Harm from Drug Interactions. Panel presentation. October 21, 2019. Capital Hilton. Washington, DC, USA.

Malone DC, Boyce RD. CDS Connect Monthly Meeting. “Using CDS to Reduce Harm From Drug-Drug Interactions: Case Study of Warfarin and Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)”. Invited Presentation to the CDS Connect community. Remote via Zoom. 6/17/2021.

Sibilla M, Malone DC, Del Fiol G, Boyce RD. Testing a Novel Tool for the Development of Drug-drug Interaction Clinical Decision Support. Accepted to the 2022 AMIA Informatics Summit. March 22 – 24, 2022. Chicago, Illinois, USA.

Products: Below are images displaying the DDInteract tool.

Figure 6. DDInteract Main View

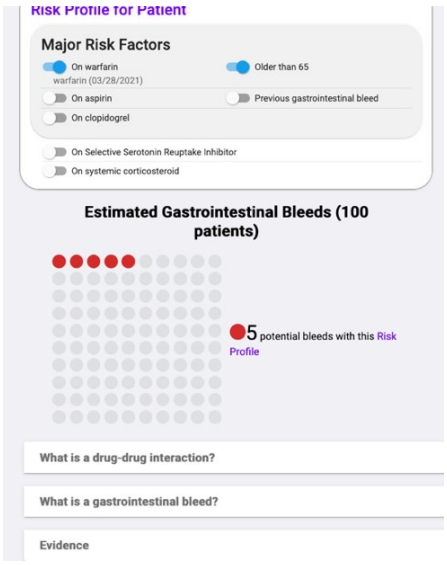


Figure 7. DDInteract Dynamic Risk Profile

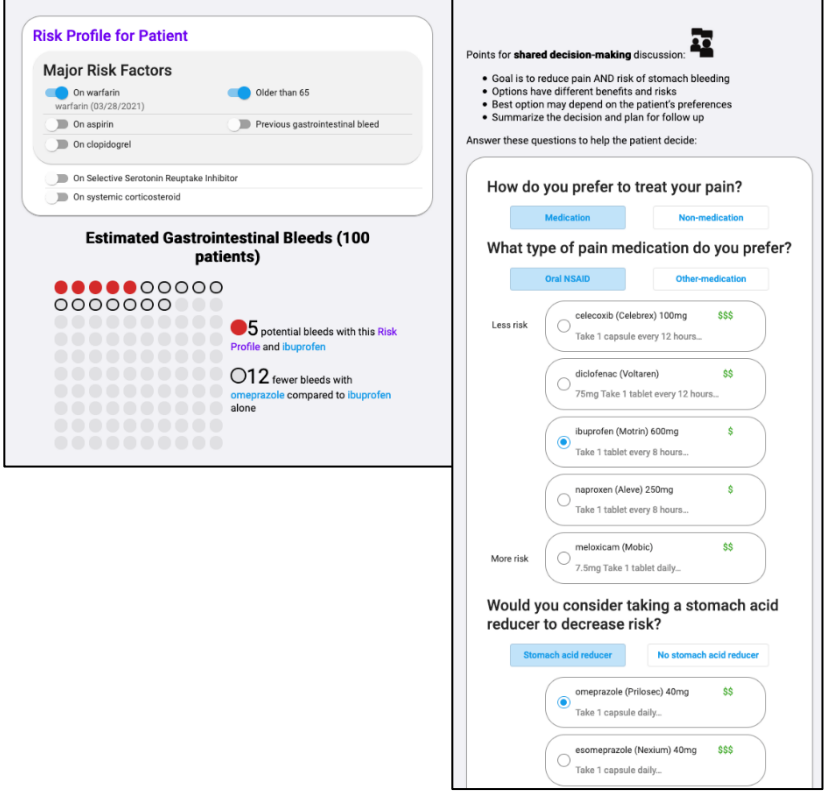


Figure 8. Overview of DDInteract App